

Conclusion: The obtained sequences may be target genes transactivated by PS1TP2 protein among which some genes coding proteins involved in cell cycle regulation, metabolism, immunity and cell apoptosis. This finding brought some clues for studying the biological functions of PS1TP2.

PP-106 Study of the association of hepatitis B surface antigen and HLA with hepatocellular carcinoma

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Introduction: Primary liver cancer accounts for only 1–2% of malignant tumors found at autopsy in western countries. However, in some parts of Africa and Asia it may account for up to 20–30% of all types of malignancy. The high frequency of HBsAg positivity in individuals with Hepatocellular Carcinoma (HCC) strongly suggests that chronic HBV infection may contribute in some way towards the development of 1st liver cell carcinoma. Although HCC is probably caused by one or more environmental carcinogens, a hereditary predisposition to the tumor has not been excluded.

Aim: Determine the incidence of HBsAg carriers patients suffering from primary HCC and detect the association between primary HCC and HLA.

Subjects and Methods: The material consisted of twenty patients diagnosed as HCC based on Ultrasonographic examination and by Histopathology. Laboratory investigations; liver biopsy, HBsAg, Anti-HBcAg (IgM) and HLA typing using lymphocyte microcytotoxicity technique.

Results: The 20 studied cases were negative for HBcAb IgM and 10 patients were positive for HBsAg. HLA typing revealed significant rise of HLA-A9, HLA-B5 among HCC patients. HLA-A9 was significantly increased in HBsAg positive and negative cases. HLA-B5 was significantly increased in HBsAg positive cases only while HLA-B8 was significantly increased in HBsAg negative cases only.

In cases with mixed hepatic cirrhosis and Schistosomal hepatic fibrosis which were negative for HBsAg showed significant increase in HLA-A9.

Conclusions:

1. Significant association of HBsAg positivity in patients with HCC.
2. Significant association of HLA-A9 and HLA-B5 with HCC.
3. HLA-A9 in patients mixed cirrhosis and Schistosomal hepatic fibrosis may be predisposing to HCC.

PP-107 Lentivirus mediated shRNA interference targeting DR1 and CP region of HBV genome stably inhibits viral replication in vitro

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RNAi is a potential tool for antiviral therapy. However, plasmid-based shRNA and chemically synthetic siRNA are ineffective in treating viral infection due to limited transfection efficiency and short half-life. Thus, non-replicating recombinant viral vectors, in particular lentiviral DNA which can integrate into host genome, may represent effective means in antiviral treatment. In order to study the kinetics of gene silencing, it is desirable to suppress genes in a regulated fashion. Such regulated RNAi system can provide a way to express shRNA only when needed or only in certain cells. Traditional anti-HBV drugs, such as

nucleoside analogues and interferon- α , are only partially effective in reducing viral loads.

Here we applied the regulated lentiviral delivery system to investigate the suppressive effect of siRNA on HBV. We compared two expression systems, a DNA-based vector (pSuper) under H1 promoter and the lentiviral vector, to deliver siRNA targeting the direct repeat 1 (DR1) region, the core promoter (CP) region or the reverse transcriptase (RT) of HBV genome. First, we designed and constructed shRNA into the pSuper vector and assessed the effect on HBV replication in HepG2.2.15 cells. We found that the shRNA targeting DR1 region (1826nt-1845nt) or the CP region (1775nt-1795nt) significantly suppressed HBV replication, while shRNA targeting RT only had moderate effect. We subsequently cloned shRNA cassettes targeting DR1 region and CP region into the lentiviral vector, respectively. Recombinant lentiviruses were transduced into HepG2.2.15 cells with 95% efficacy as evidenced by fluorescence microscopy, resulting in great reduction at both mRNA and protein levels which were maintained to 96h post-transduction.

We are currently constructing the tetracycline operator system into the lentiviral vector to generate a tetracycline based-regulated RNAi system. This conditional RNAi system will provide a promising tool to analyze siRNA-mediated anti-HBV therapy.

PP-108 Prevalence of transfusion-transmitted virus in patients with viral liver disease

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Aim: To explore the prevalence of transfusion transmitted virus (TTV) infection in patients with viral liver diseases.

Methods: TTV DNA in serum from all enrolled patients with viral liver disease (VLD) was detected with PCR method. Anti-HAV, HBV-marker, anti-HCV, anti-HDV and anti-HEV markers were also tested by ELISA. HBV DNA, HCV RNA and HGV RNA were detected by PCR and RT-PCR method.

Results: The prevalence rate of TTV infection in VLD patients was 14.7% (43/292). Of all the patients, the percentage of TTV infection was 5.0% (2/40), 15.9% (29/182), 31.6% (6/19) and 11.8% (6/51), respectively in patients with acute hepatitis (AH), chronic hepatitis (CH), severe hepatitis (SH) and liver cirrhosis (LC); in which the rate of TTV infection with SH predominated ($p < 0.001$). Of all the 43 patients with positive TTV in serum, 5 (11.6%) cases were infected with TTV alone, 38 (88.4%) patients were super-infected with more than one hepatitis virus (HV). The double infection rate was significantly higher than the single infection rate ($p < 0.01$). In the group infected with TTV, there were 2 AH cases (4.7%), 29 CH cases (67.4%), 6 SH cases (14.0%) and 6 LC cases (14.0%), and in which CH predominated ($p < 0.01$). In AH group, 2 cases infected with TTV, 1 with TTV only, another one was super-infected with other HV. In CH group (29), 3 with TTV single infection, 26 with TTV super-infection. In SH group, 1 was with TTV single infection, 5 with TTV super-infected. In LC group, all patients were TTV super-infected. In the group infected with TTV only, most patients had the symptoms of CH (60%). In the group super-infected with HV, most patients were super-infected with HBV (89.5%, 34/38). The super-infection group was composed of AH, CH, SH and LC (2.6%, 68.4%, 13.2%, and 15.8% respectively).

Conclusions: TTV infection is common in patients with viral liver disease. TTV is frequently super-infected with other

HV, especially HBV and HCV, and it seems to be related to the pathogenicity of cirrhosis and fulminant hepatic failure.

PP-109 Usefulness of the serum concentrations of TIMP-1 and TIMP-2 for predicting liver fibrosis in patients with chronic hepatitis B

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Objectives: We determined whether serum concentration of TIMP-1 and TIMP-2 are related to the progress of liver fibrosis in patients with chronic hepatitis B (CHB).

Methods: Commercially available ELISA were used to study circulating values of TIMP-1 and TIMP-2 in CHB patients (n=159) and 20 healthy controls. TIMP-1 and TIMP-2 expressions in the liver were detected by immunohistochemical staining, then analyzed the correlation between the levels of hepatic expression and serum concentration of them. Hepatic histology was evaluated, and quantified the stage of fibrosis by using the Hepatitis-Activity-Index (HAI) according to Ishak et al.

Results: The serum concentration of TIMP-1 or TIMP-2 positively correlated with their expression in the liver of CHB patients, and both of them were higher in the patients than those in the healthy controls, and which had a significant difference ($P < 0.05$). The serum concentrations of TIMP-1 and TIMP-2 increased significantly with development of fibrosis and had positive correlations with HAI ($r = 0.51$, $P < 0.01$; $r = 0.42$, $P < 0.01$), whereas serum ALT wasn't related to fibrosis or HAI.

Conclusions: Regular determinations of both TIMP-1 and TIMP-2 in CHB patients may be used as indicators of increasing fibrosis.

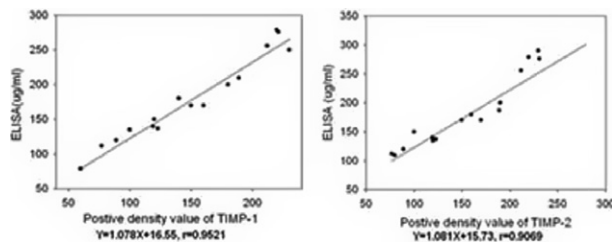


Figure 1. Correlation between TIMP-1 and -2 expressions in the liver and their concentration in the serum of patients with CHB.

Table 1. The serum concentration of TIMP-1 and -2 in CHB patients with different stages of fibrosis

	TIMP-1 (μg/L)	TIMP-2 (μg/L)	ALT (IU/L)
S0	84.32±18.53	52.34±24.21	45.37±9.31
S1	109.32±14.67	108.96±12.56	105.54±8.59
S2	135.65±22.95	111.47±25.32	676.4±202.35
S3	181.05±39.44	178.28±17.76	432.2±273.88
S4	279.91±61.83	255.54±110.02	75.7±29.80

PP-110 A study of the carriers of hepatitis B surface antigen among patients with schistosomal hepatic fibrosis

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Introduction: Hepatitis B virus infection is recognized as a major public health problem causing acute, persistent

or chronic liver infection. In Egypt, hepatitis B virus infection is considered to be endemic. The attack rate of hepatitis B was estimated to reach 8.9/10,000 in Alexandria. Schistosomiasis is considered the major health problem in Egypt. 12–14 million people are infected with *Schistosoma mansoni*.

When Schistosomal and non-Schistosomal patients were exposed to HBV, they were found to be equally susceptible, however follow-up studies claimed that the first group of patients tend to exhibit hepatitis B antigenemia for longer periods than the second group and this may hugely increase the reservoir of carriers.

Aim: Determine the prevalence of HBsAg carriers, demonstration of routes of antigen excretion and its presence in liver sections and the prevalent subtype.

Subjects and Methods: Forty carriers of the hepatitis B surface antigen were selected from 539 cases of Schistosomal hepatic fibrosis:

A. Detection of HBsAg in patients sera, Saliva, Urine and Stools & Anti-HBcAg IgM.

B. Demonstration of HBsAg in infected hepatocytes.

C. Subtyping of HBsAg using the counter immuno-electrophoresis.

Results:

- Hepatitis B surface antigen carriers was 7.42%, Anti-HBsAg IgM was negative.
- 5% of the salivary samples were HBsAg positive, while 50% of the Urine and Stool were HBsAg positive.
- Urine and Saliva positivity ran parallel.
- Stool samples positive for HBsAg were all positive for occult blood.
- Subtyping of the HBsAg for showed the "ay" subspecificity which is considered the constant type of North Africa.

Conclusions:

- Screening of Schistosomal patients for the HBs antigen is of importance as they represent a highly disseminating source of infection.
- "ay" is the predominant subtype of HBs Ag.
- Disinfection of secretions and excretions of HBsAg positive patients and their utensils is essential.

PP-111 Optimal threshold: baseline serum hepatitis B virus DNA and alanine transaminase levels predict the 2-year on-treatment virological response to lamivudine

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Aims: To evaluate the predictive value of baseline levels of HBV DNA and ALT for the long term efficacy of lamivudine treatment for patients with chronic hepatitis B and determine the optimal cut off values of baseline levels of HBV DNA and ALT.

Methods: A total of 163 HBeAg-positive chronic hepatitis B patients receiving LAM treatment were recruited into the present study. Logistic regression analysis was performed to screen independent predictors of 2-year on-treatment virological response among the baseline parameters. The ROC curve was used to evaluate the predictive value of these independent predictors. The accuracy of prediction was assessed using area under curve (AUC) and optimal cut off values were determined through maximizing Youden's index.

Results: After 2 years of LAM treatment, HBV DNA was undetectable in 114 (69.9%) patients and LAM related resistance mutation was detectable in 45 (27.6%) patients. Logistic regression analysis indicated the baseline levels of ALT and HBV DNA were the independent predictors